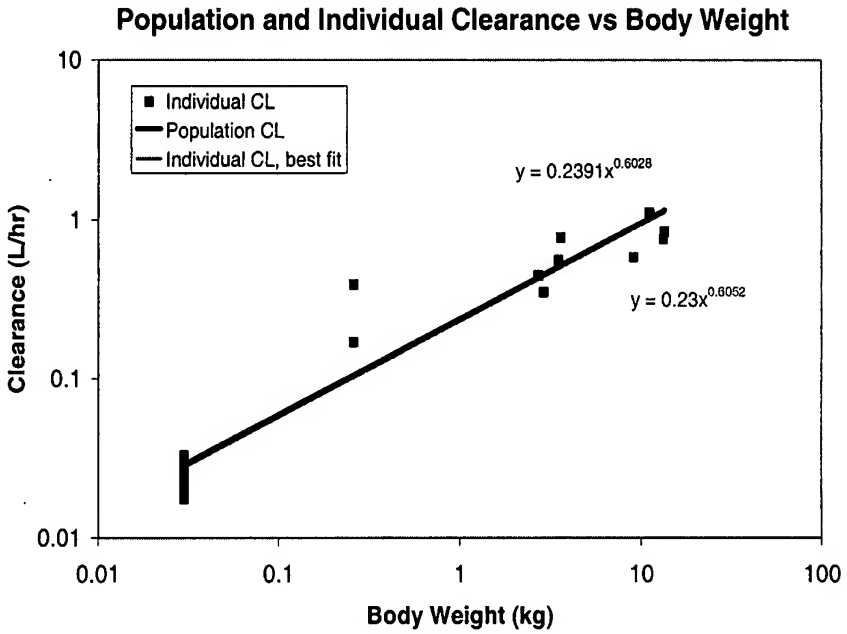
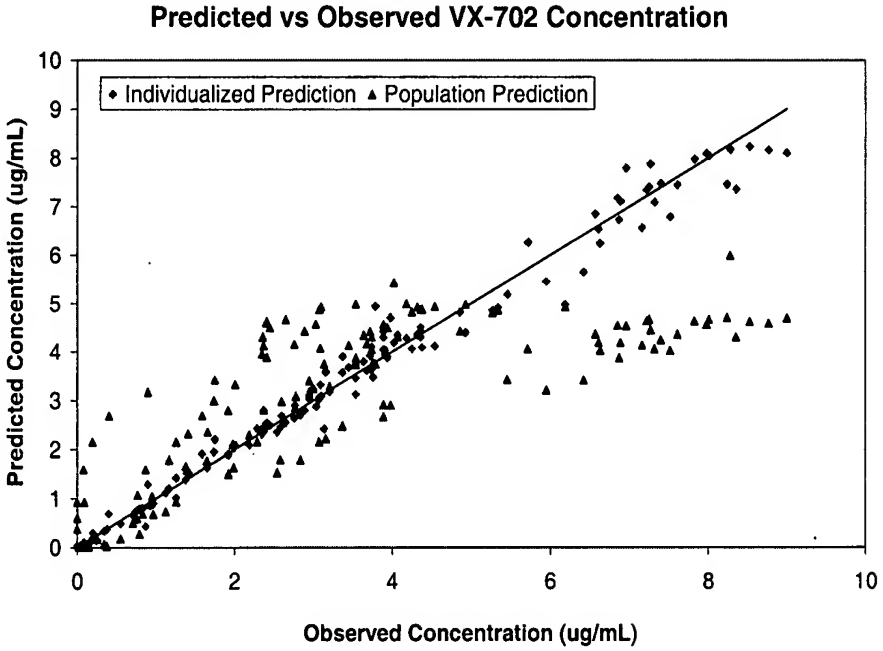
FIGURE 1



Population predictions of concentration are derived from population PK parameter estimates, individual predictions are based on empirical Bayesian estimates of PK parameters.

FIGURE 2



Population predictions of concentration are derived from population PK parameter estimates, individual predictions are based on empirical Bayesian estimates of PK parameters.

FIGURE 3

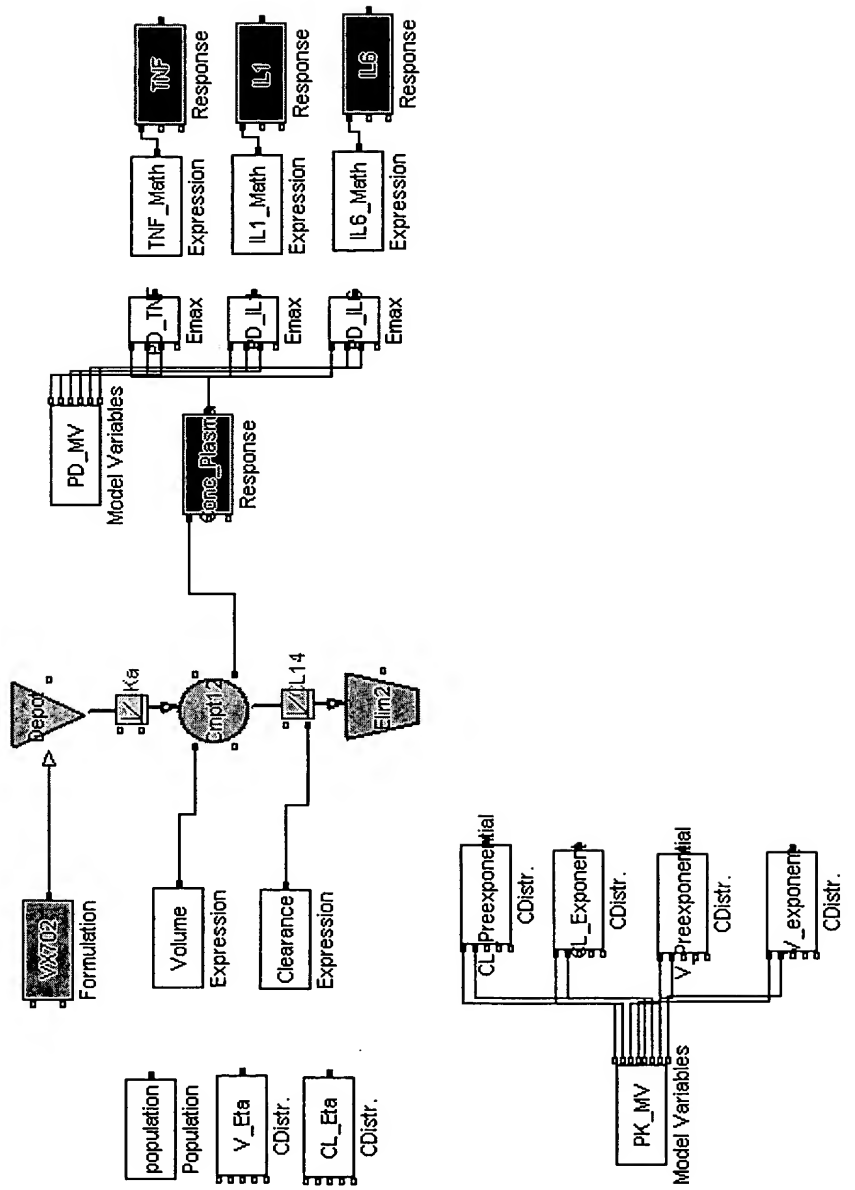
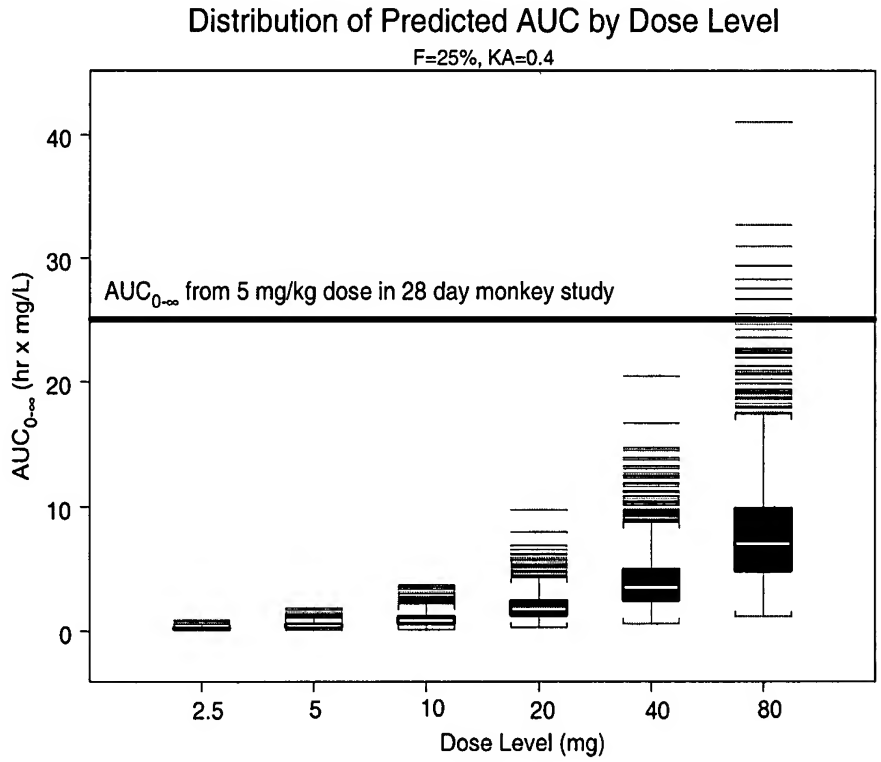
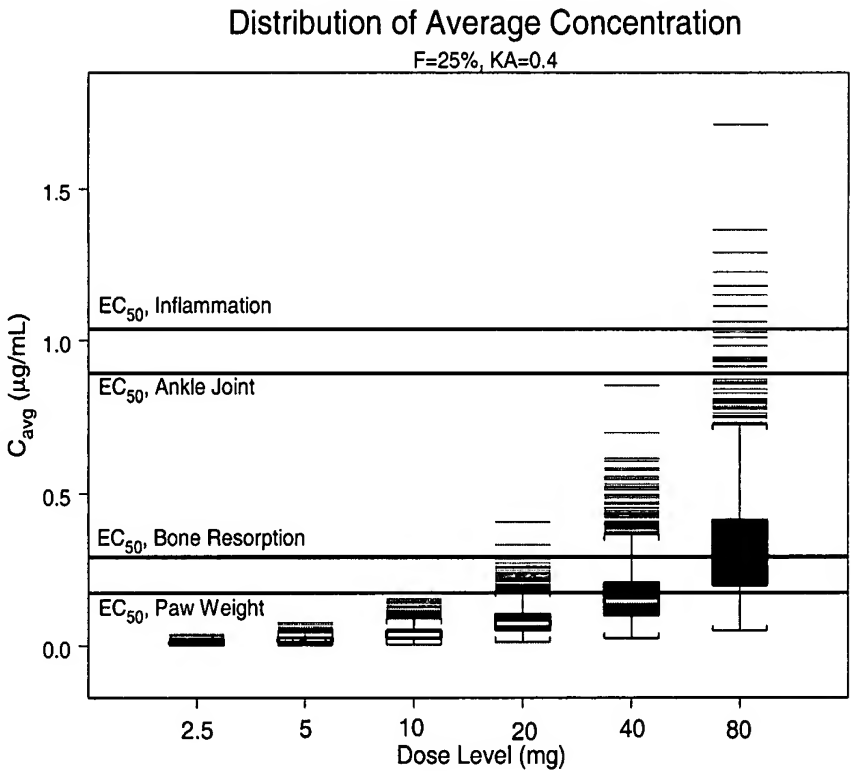

TNF
Response
IL1
Response
IL6
Response
TNF_Math
Expression
IL1_Math
Expression
IL6_Math
Expression
PD_TNF
Emax
PD_IL1
Emax
PD_IL6
Emax
PD_MV
Model Variables
Cone_Plasma
Response
Depot
Ka
Cmpt1
L14
Elim2
VX702
Formulation
Volume
Expression
Clearance
Expression
population
Population
V_Eta
CDistr.
CL_Eta
CDistr.
CL_Preexponential
CDistr.
CL_Exponent
CDistr.
V_Preexponential
CDistr.
V_exponent
CDistr.
PK_MV
Model Variables

FIGURE 4



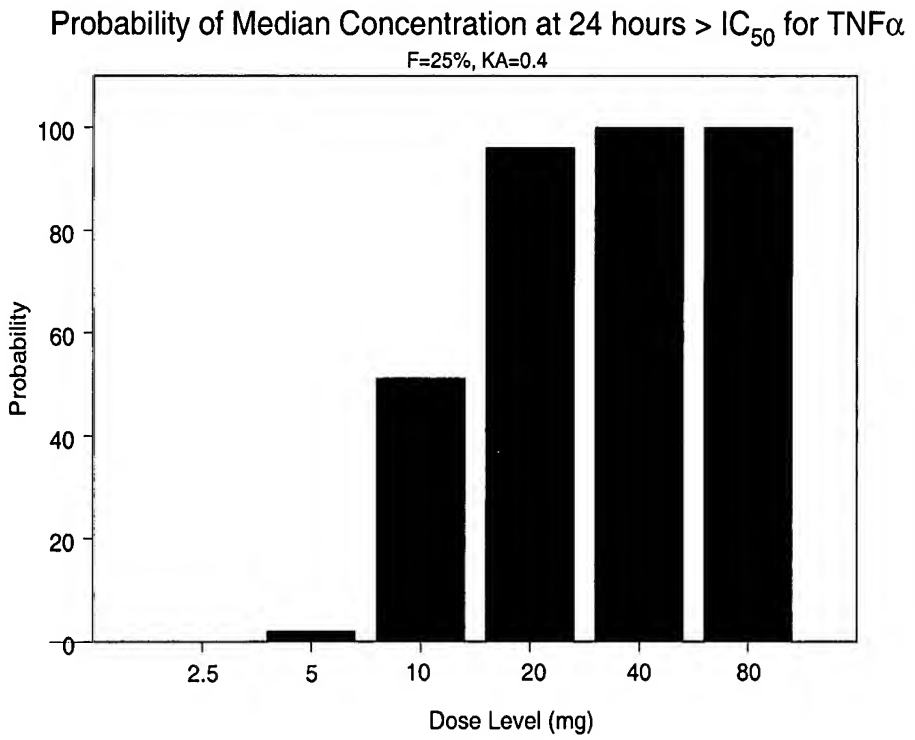
The distribution of $AUC_{0-\infty}$ for the starting dose of 2.5 mg and over the escalation scheme is depicted in relation to the NOAEL exposure in the 28-day repeat dose oral toxicity study in monkeys. The distribution incorporates expected variability as well as uncertainty associated with allometric extrapolation of animal PK to humans.

FIGURE 5



This figure depicts the relationship between the distribution of average concentrations and EC_{50}s determined in the adjuvant-induced arthritis model in rats.

FIGURE 6



The probability of the predicted median concentration 24 hours post-dose exceeding the TNFα IC_{50} from the in vitro LPS stimulated cytokine production in whole blood assay.